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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,330	04/14/2005	Toshihiro Hosaka	0283-0211PUS1	7849

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EXAMINER

YOUNG, SHAWQUA

ART UNIT	PAPER NUMBER
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1626

NOTIFICATION DATE	DELIVERY MODE
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09/06/2007

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/531,330

Applicant(s)

HOSAKA, ET AL.

Examiner

Shawquia Young

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 10-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 24 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/14/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-25 are currently pending in the instant application.

I. *Priority*

The instant application is a 371 of PCT/JP03/13194, filed on October 15, 2002 and claims benefit of Foreign Applications JP 2002-300860, filed on October 15, 2002 and JP 2003-104260, filed on April 8, 2003.

II. *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on April 14, 2005 is in partial compliance with the provisions of 37 CFR 1.97 for missing copies of references in the foreign documents section. Accordingly, the information disclosure statement has been partially considered by the examiner.

III. *Restriction/Election*

A. Election: Applicant's Response

Applicants' election with traverse of Group I in the reply filed on July 9, 2007 is acknowledged. The traversal is on the ground(s) that: (1) that unity of invention exists for all of the present claims..

All of the Applicants' arguments have been considered but have not been found persuasive. It is pointed out that the restriction requirement is made under 35 U.S.C. 121. 35 U.S.C. 121 gives the Commissioner (Director) the authority to restrict applications to several claimed inventions when those inventions are found to be independent and distinct. The Examiner has indicated that more than one independent

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514 contained 165,171 patents and published applications. Therefore it would constitute a burden on the Examiner and the Patent Office's resources to examine the instant application in its entirety.

Subject matter not encompassed by elected Group II are withdrawn from further consideration pursuant to 37 CFR 1.142 (b), as being drawn to nonelected inventions.

IV. Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9,24 and 25 are rejected under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first

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and distinct invention is claimed in this application and has restricted the claimed subject matter accordingly.

Applicants argue that the reference cited by the Examiner (Katz, et al.) relates to organic semiconductors and does not relate to the present claims. Applicants further argue that the present claims do not recite the compounds disclosed in the Katz, et al. reference and that it cannot be maintained that the reference discloses the special technical feature of the present claims which defines a contribution over the prior art. The Examiner wants to point out that the reference is not being used as a prior art rejection, it is being used to show applicants that the special technical feature in the claimed invention does not provide a contribution over the prior art. Therefore it is not necessary for the reference to teach the same utility as applicants' claimed invention. Applicants' claims do not have unity of invention because the special technical feature which all the claims have in common is drawn to the compound of formula I. The special technical feature is a five-membered heterocyclic ring. As shown in applicants' claims, the five-membered heterocyclic ring can be heterocyclic rings such as furanyl, thienyl, etc. These heterocyclic rings are classified differently and therefore are distinct.

The Restriction Requirement detailed the reasons for restriction between the groups. Different search considerations are involved (i.e., class/subclass searches, databases searches, etc.) for each of the groups listed. The inventions are classified into classes 514, 544, 546, 548 and 549. However, each Class 514, 544, 546, 548 and 549 encompasses numerous patents and published applications. For instance, Class

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paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case

The nature of the invention

The nature of the invention is a method for prophylaxis or treatment of a disease against which a large conductance calcium-activated K channel opening activity is efficacious.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is

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the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of any condition mediated by a large conductance calcium-activated K channel opening activity, whether or not the condition is effected by the activity would make a difference.

Applicants are claiming a method for prophylaxis or treatment of a disease against which a large conductance calcium-activated K channel opening activity is efficacious.

Applicants' claims are therefore drawn to a method for prophylaxis or treatment of a disease such as diabetes, irritable bowel syndrome, angina, chronic heart failure, urinary incontinence, pollakiuria, etc.

Diabetes, also known as diabetes mellitus, is defined as impaired insulin secretion and variable degrees of peripheral insulin resistance leading to hyperglycemia. Early symptoms are related to hyperglycemia and include polydipsia, polyphagia and polyuria. Later complications include vascular disease, peripheral neuropathy and predisposition to infection. There are two main categories of diabetes mellitus-type 1 and type 2. Treatment involves control of hyperglycemia to improve symptoms and prevent complications while minimizing hypoglycemic episodes. Oral antihyperglycemic drugs are the primary treatment for type 2 diabetes mellitus. However, there are no treatments that definitely prevent the onset or progression of type 1 diabetes mellitus.

<http://www.merck.com/mmpe/print/sec12/ch158/ch158b.html>

Applicants are also claiming the treatment or prophylaxis of Irritable bowel syndrome. Irritable bowel syndrome (IBS) is a common problem with the intestines. It is when the intestines squeeze too hard or not hard enough and cause food to move too quickly or too slowly through the intestines. There is no cure for IBS, but medicine can help to manage or lessen your symptoms. Common symptoms include bloating and gas, mucus in the stool, constipation, abdominal pain, diarrhea, etc. Antispasmodic medicines may be prescribed to reduce cramping if your main symptom is pain. When diarrhea is a frequent problem, anti-diarrhea medicine such as loperamide may help. Therefore, treatment of irritable bowel syndrome is based upon what symptoms the patient in need has.

(<URL:<http://familydoctor.org/online/famocen/home/common/digestive/disorders/112.html>>)

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. The specification only gives a list of conditions mediated by the opening of a large conductance calcium-activated K channel. There are only a few working examples present for the treatment of urinary incontinence.

Test assays and procedure are provided in the specification at pages 67-70 such as the relaxation effect on potassium-induced contraction of isolated rabbit urinary bladder and inhibitory effect on the rhythmic bladder contractions induced by substance

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P in rats. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is a method for prophylaxis or treatment of a disease against which a large conductance calcium-activated K channel opening activity is efficacious.

Furthermore, the instant claims cover "diseases" that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

The quantity of experimentation needed and the level of the skill in the art

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases would be benefited by the effects of the opening of a large conductance calcium-activated K channel and would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of the diseases.

The level of skill in the art is high. However, due to the unpredictability in the

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pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the broad method claims.

V. Objections

Dependent Claim Objections

Dependent Claim 24 is also objected to as being dependent upon a non-elected claim. To overcome this objection, Applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim.

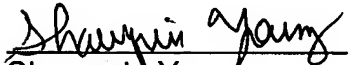
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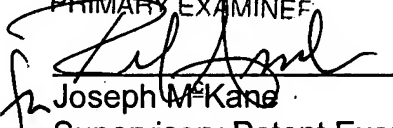
VI. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 6:30 AM-3:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^{re}Kane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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